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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,038	06/08/2005	Jay Patrick Slack	102790-135 (30069 US/2)	1345

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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
05/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,038	SLACK ET AL.	
	Examiner	Art Unit	
	Scott D. Long	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-13 and 18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-13 and 18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 March 2008 has been entered.

Claim Status

Claims 1 and 6-8 are amended. Claims 3-5 and 14-17 are cancelled. Claims 18-34 are newly presented. Claims 1-2, 6-13, and 18-34 are under current examination.

Priority

This application claims benefit as a 371 of PCT/CH03/00830 (filed 12/17/2003) which claims benefit of 60/434,790 (filed 12/18/2002). The instant application has been granted the benefit date, 18 December 2002, from the application 60/434,790.

Response to Claim Objections

The applicant has amended claims 6-8 to include "SEQ ID NO:" This amendment satisfies the examiner's objection. Therefore, the examiner hereby withdraws the objections to claims 5-8.

Response to Arguments - Claim Rejections 35 USC § 112

Response to Arguments – 35 USC 112, first paragraph

Applicant's arguments (Remarks, pages 7-12) and Claim amendments, filed 20 March 2008, with respect to claims 1-2 and 10-13 have been fully considered and are persuasive.

The applicant has amended claim 1 to specify a particular amino acid sequence (i.e., last 44 amino acids of SEQ ID NO:2) to replace the last 44 amino acids of $G_{\alpha q}$ protein. There is no ambiguity about the structure claimed. Furthermore, the specification contains support for this structure.

Therefore, the rejection of Claims 1-2 and 10-13 under 35 USC 112, first paragraph (written description), is hereby withdrawn.

Response to Arguments - Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, and 10-13 remain rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

Claim 1 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants…may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity id of particular importance because it

encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 of SEQ ID NO:2 of the instant application.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit.

Yao et al. teach "chimeric G_q variants and th isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, claim 1 would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

Claim 2 is directed to the chimeric protein of claim 1, wherein the G-protein is a $G_{\alpha 15 \text{ or } 16\text{-Gustducin}}$. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4).

Claim 10 is directed to methods of producing a chimeric G-protein of claim 1 by recombinant technology. Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24).

Claim 11 is directed to a method of analysis and discovery of modulators of bitter taste receptors using the chimeric proteins of claim 1. Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56).

Claims 12-13 directed to a method of claim 11, wherein the assay is a mammalian cell-based assay. Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

Margolskee does not specifically teach the $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein and also does not specifically recited replacement of the C-terminal sequence 44 amino acids of the gustducin receptor.

Yao et al. teach, $G_{\alpha q}$ chimeric G-proteins (col.4, lines 12-27). In particular, the chimeric proteins described, combine various $G\alpha_q$ class proteins. Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13).

Yao et al. also teach analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants (col.3, lines 15-30), including the "gustducin-coupled bitter receptor" (col.4, line 53). Yao et al. further suggest that modulators could be used in "protein pharmaceutical and food industries" (col.4, line 32). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Consequently, claims 3-4 would be obvious, in light of the teachings of Yao et al.

Ruiz-Avila et al. teach the nexus of gustducin and transducin homology and the importance of the C-terminus for interacting with taste receptors.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make a $G\alpha_{q\text{-Gustducin}}$ chimeric G-protein having a C-terminal 44 amino acid substitution from Gustducin.

The person of ordinary skill in the art would have been motivated to make this protein because, "C-terminal substitution increases promiscuity of said variant G, protein as compared to the corresponding native G_q protein" (Yao et al. col.5, lines 20-22). While Yao et al. does not specifically teach making a chimera between G_q protein and gustducin, it is clearly obvious in light of the teachings involving substitutions with C-terminal sequences from other chemosensory molecules, transducin and $G\alpha_{olf}$). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Additionally, Margolskee teach that the carboxy terminal 40 amino acids of Gustducin are important for G protein/receptor interactions. Furthermore, Margolskee teach "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical." Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). Furthermore, Yao et al. suggest that analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants can be performed using chimeric proteins and actually mention gustducin bitter receptor as a receptor which might be useful "to customize sensory perception" (col.4, line 32-33).

An artisan would have expected success, because Yao et al. were successful in making similar chimeric G-proteins with other chemosensory receptors.

Therefore the products and method as taught by Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al. would have been *prima facie* obvious over the method of the instant application.

Applicant's arguments (Remarks, pages 12-15) and claim amendments, filed 20 March 2008, with respect to rejection of claims 1-2 and 10-13 under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873) have been fully considered but are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). For example, the applicant asserts, "The first two cited references have already been overcome on the record. Thus, the only additional art is Ruiz-Avila et al." (Remarks, page 13) and "Margolskee merely discloses Gustducin, but no chimeric G-protein. Ruiz-Avila et al. is also not directed to chimeric G-proteins....Ruiz-Avila et al...does not suggest anything in terms of actual functionality...in a chimeric protein" and "an artisan would therefor not be motivated to make the claimed chimeric G-protein, nor would have expected success based on Yao et al. chimeric G-proteins" (pages 14-

15). It is the combination of references which makes the instantly claimed invention obvious (as recited above in the text of the rejection). The applicant's arguments are spurious and unpersuasive.

The applicant has not pointed out why the references are not combinable. Furthermore, the applicant has not pointed out which limitations are not taught by the prior art. The examiner has explained (1) Yao et al. teach a chimeric G_q-protein wherein the C terminus is replaced by 44 amino acids of transducin; (2) Margolskee specifically teach the 40 amino acid carboxy terminal end of gustducin and the homologies between the C-termini of gustducin and transducin; and (3) Ruiz-Avila et al. teach that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. Together these references render obvious a chimeric Gα-protein wherein the 44 amino acid C-terminus comprises the c-terminal 44 amino acids of gustducin.

Therefore, the examiner hereby maintains the rejection of Claims 1-2 and 10-13 under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873)..

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6-13, and 18-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

Claim 1 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2.

Claim 18 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2 and wherein the resulting $G_{\alpha q\text{-}Gust44}$ chimeric G-protein has a sequence homology of at least 80% in the last 44 amino acids of SEQ ID NO:2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants...may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 amino acids of SEQ ID NO:2 of the instant application. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4). Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host

cells comprising the expression vector (col.3, line 24). Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56). Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit. Margolskee does not specifically teach the $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein and also does not specifically recite replacement of the C-terminal sequence 44 amino acids of the gustducin receptor.

Yao et al. teach "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase

promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Yao et al. teach, $G_{\alpha q}$ chimeric G-proteins (col.4, lines 12-27). In particular, the chimeric proteins described, combine various $G\alpha_q$ class proteins. Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13).

Yao et al. also teach analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants (col.3, lines 15-30), including the "gustducin-coupled bitter receptor" (col.4, line 53). Yao et al. further suggest that modulators could be used in "protein pharmaceutical and food industries" (col.4, line 32). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Consequently, claims 3-4 would be obvious, in light of the teachings of Yao et al.

While Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13) and Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors, Yao et al. does not specifically teach a $G\alpha_{q\text{-}Gustducin}$ chimeric G-protein having a C-terminal 44 amino acid substitution from Gustducin.

Ruiz-Avila et al. teach the nexus of gustducin and transducin homology and the importance of the C-terminus for interacting with taste receptors. Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, all of the instant claims would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin.

The person of ordinary skill in the art would have been motivated to make this protein because, "C-terminal substitution increases promiscuity of said variant G, protein as compared to the corresponding native G_q protein" (Yao et al. col.5, lines 20-22). While Yao et al. does not specifically teach making a chimera between G_q protein and gustducin, it is clearly obvious in light of the teachings involving substitutions with C-terminal sequences from other chemosensory molecules, transducin and $G\alpha_{olf}$). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Additionally, Margolskee teach that the carboxy terminal 40 amino acids of Gustducin are important for G protein/receptor

interactions. Furthermore, Margolskee teach "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical." Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). Furthermore, Yao et al. suggest that analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants can be performed using chimeric proteins and actually mention gustducin bitter receptor as a receptor which might be useful "to customize sensory perception" (col.4, line 32-33).

In addition, to the strong suggestion to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin by the combined teachings of Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al., there is another rationale for combining prior art elements according to known methods to yield predictable results. All of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (chimeric $G\alpha_q$-proteins and methods of using them; a suggestion of the importance of the c-terminal 44 amino acids of Gustducin and related G-proteins;

knowledge that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors; and the knowledge that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors) are taught by Margolskee or Yao or Ruiz-Avila et al. It would be therefore predictably obvious to use a combination of these elements in a vaccine. The methods of using these chimeric G-proteins are further known in the art and are predictable; therefore they are likewise obvious.

An artisan would have expected success, because Yao et al. were successful in making similar chimeric G-proteins with other chemosensory receptors. Absent evidence to the contrary, there is no reason to believe that making a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin would not be successful.

Therefore the products and methods as taught by Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Janet L. Epps-Ford/

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